In the Claims

Please cancel claims 2-9, 14, 18-23, 26-28, 34, 46, and 47 and amend claims 1, 10, 11, 13, 29, 30, 32, 33, 35-37, 40-42, 45, 48, 49, 83, and 84 as follows:

1. (Currently amended) A method for detecting modulators of Notch ~~or immune signalling~~ signal transduction comprising the steps of (in any order):

(a) activating T-cells;

~~(a)~~(b) activating Notch signalling in ~~a cell of the immune system~~ the T-cells;

~~(b)~~(c) contacting the ~~cell~~ T-cells with a candidate modulator of Notch ~~or immune signaling~~ signal transduction;

~~(c)~~(d) monitoring ~~Notch or immune signaling~~ levels of one or more cytokines produced by the activated T-cells, wherein the cytokines are selected from the group comprising IL-5, IL-10, IL-13, and IFN gamma; and

~~(d)~~(e) ~~determining whether the candidate modulator modulates Notch or immune signaling~~ detecting a change in the level of one or more cytokines in the presence of the candidate modulator as compared to the cytokine level in the absence of the modulator, wherein a change in the level of one or more cytokines indicates the candidate modulator alters Notch signal transduction.

2-9. (Cancelled)

10. (Currently amended) The method of claim 1, wherein ~~immune cell~~ T-cell activation is at least 20% optimal with respect to Notch ~~or immune signalling~~ signal transduction.

11. (Currently amended) The method of claim 1, wherein ~~immune cell~~ T-cell activation is at least 70% optimal with respect to Notch ~~or immune signalling~~ signal transduction.

12. (Original) The method of claim 1, wherein the candidate modulator is selected from the group consisting of an organic compound, an inorganic compound, a peptide, a polypeptide, a polynucleotide, an antibody, a fragment of an antibody, a cytokine and a fragment of a cytokine.

13. (Currently amended) The method of claim 1, wherein monitoring ~~Notch signalling~~ the levels of one or more cytokines comprises monitoring expression levels ~~of at least one target gene~~.

14. (Cancelled)

15. (Withdrawn) The method of claim 13, wherein the at least one target gene is selected from the group consisting of CBF-1, Hes-1, Hes-5, E(spl), IL-10, CD-23, Dlx-1, CTLA4, CD-4, Numb, Mastermind and Dsh.

16. (Withdrawn) The method of claim 13, wherein the at least one target gene is a reporter gene.

17. (Withdrawn) The method of claim 16, wherein the reporter gene is selected from the group consisting of a gene encoding a polypeptide having an enzymatic activity, a gene comprising a radiolabel or a fluorescent label, and a gene encoding a predetermined polypeptide epitope.

18-23. (Cancelled)

24. (Withdrawn) The method of claim 22, wherein the signalling pathway specific to cells of the immune system is a B cell receptor (BCR) signalling pathway.

25. (Withdrawn) The method of claim 22, wherein the signalling pathway specific to cells of the immune system is a Toll-like receptor (TLR) signalling pathway.

26-28. (Cancelled)

29. (Currently amended) The method of claim 13, wherein cytokine expression ~~of the at least one target gene~~ is monitored with a protein assay.

30. (Currently amended) The method of claim 13, wherein cytokine expression ~~of the at least one target gene~~ is monitored with a nucleic acid assay.

31. (Original) The method of claim 1, wherein Notch signalling is activated by (i) activating Notch, (ii) providing a constitutively active truncated form of Notch, or (iii) providing an active Notch IC domain.

32. (Currently amended) The method of claim 1, wherein the candidate modulator has a molecular weight of less than about 1000 Daltons.

33. (Currently amended) The method of claim 1, wherein the candidate modulator has a molecular weight of less than about 500 Daltons.

34. (Cancelled)

35. (Currently amended) The method of claim [[34]] 1, wherein the T-cell is activated by activation of a T-cell receptor.

36. (Currently amended) The method of claim [[34]] 1, wherein the T-cell is activated with an antigen or antigenic determinant.

37. (Currently amended) The method of claim [[34]] 1, wherein the T-cell is activated by an anti-CD3 antibody or an ~~anti-TCR~~ anti-T-cell receptor (TCR) antibody.

38. (Original) The method of claim 37, wherein the anti-CD3 antibody or anti-TCR antibody is bound to a support.

39. (Original) The method of claim 38, wherein the support is a particulate support.

40. (Currently amended) The method of claim [[34]] 1, wherein the T-cell is activated with a calcium ionophore.

41. (Currently amended) The method of claim [[34]] 1, wherein the T-cell is activated with an activator of protein kinase C or MAP Kinase.

42. (Currently amended) The method of claim [[34]] 1, wherein the T-cell is co-activated.

43. (Original) The method of claim 42, wherein the T-cell is co-activated by activation of CD28.

44. (Original) The method of claim 43, wherein activation of CD28 is by an anti-CD28 antibody or a CD28 ligand.

45. (Currently amended) The method of claim 42, wherein the T-cell is activated by an anti-CD3 antibody or ~~and~~ an anti-TCR antibody, and co-activated by an anti-CD28 antibody or a CD28 ligand.

46-47. (Cancelled)

48. (Currently amended) The method of claim 1, wherein the ~~immune cell~~ T-cell is transfected with an expression vector encoding (i) Notch, (ii) a constitutively active truncated form of Notch, or (iii) a Notch IC domain.

49. (Currently amended) The method of claim 1, wherein the ~~immune cell~~ T-cell is transfected with a Notch reporter construct.

50. (Withdrawn) A modulator of Notch identified by the method of claim 1.

51. (Withdrawn) A composition comprising a therapeutically effective amount of at least one modulator according to claim 50 and a pharmaceutically acceptable carrier, diluent and/or excipient.

52. (Withdrawn) A method of treating a disease or condition of, or related to, the immune system comprising administering the composition of claim 51 to a subject in need thereof.

53. (Withdrawn) The method of claim 52, wherein the disease is a T-cell mediated disease.

54. (Withdrawn) The method of claim 52, wherein the disease is a B-cell mediated disease.

55. (Withdrawn) The method of claim 52, wherein the disease is an APC mediated disease.

56. (Withdrawn) The method of claim 1, wherein Notch signalling is activated with a Notch ligand.

57. (Withdrawn) The method of claim 56, wherein the Notch ligand is presented on a cell or cell membrane.

58. (Withdrawn) The method of claim 56, wherein the Notch ligand is bound to a support.

59. (Withdrawn) A particle comprising protein comprising a Delta DSL domain and at least one Delta EGF domain bound to a particulate support matrix.

60. (Withdrawn) A particle comprising a protein comprising a Delta extracellular domain, or an active portion thereof, bound to a particulate support matrix.

61. (Withdrawn) The particle of claim 59, wherein the particulate support matrix is a bead.

62. (Withdrawn) The particle of claim 60, wherein the particulate support matrix is a bead.

63. (Withdrawn) The particle of claim 59, wherein a plurality of proteins comprising a Delta DSL domain and at least one Delta EGF domain are bound to the particulate support matrix.

64. (Withdrawn) The particle of claim 60, wherein a plurality of proteins comprising a Delta extracellular domain, or an active portion thereof, are bound to the particulate support matrix.

65. (Withdrawn) A method for identifying genes which are upregulated in an immune cell in response to a combination of Notch signalling and immune cell activation comprising the steps of (in any order):

(a) activating an immune cell;

(b) activating Notch signalling in the cell;

(c) monitoring gene expression; and

(d) determining which genes are upregulated,

thereby identifying genes which are upregulated in an immune cell in response to a combination of Notch signalling and immune cell activation.

66. (Withdrawn) A method for identifying genes which are upregulated or downregulated in an immune cell to a greater extent in response to a combination of Notch signalling and immune cell activation than in response to Notch signalling or immune cell activation alone, the method comprising the steps of (in any order):

(a) activating an immune cell;

(b) activating Notch signalling in the cell;

(c) monitoring gene expression;

(d) determining whether gene expression is upregulated or downregulated in the cell; and

(e) comparing gene expression from step (d) with gene expression in a cell that is not activated or wherein Notch signalling is not activated,

thereby identifying genes which are upregulated or downregulated in an immune cell to a greater extent in response to a combination of Notch signalling and immune cell activation than in response to Notch signalling or immune cell activation alone.

67. (Withdrawn) The method of claim 65, wherein gene expression is monitored using a microarray.

68. (Withdrawn) The method of claim 65, wherein the immune cell is a T-cell.

69. (Withdrawn) A gene identified by the method of claim 65.

70. (Withdrawn) An assay for identifying a compound that modulates Notch siganlling comprising the steps of (in any order):

(a) providing a culture of immune cells;

(b) transfecting said cells with a Notch signalling reporter construct;

(c) optionally transfecting said cells with a nucleic acid encoding (i) Notch, (ii) a constitutively active truncated form of Notch or (iii) a Notch IC domain;

(d) optionally providing a Notch ligand;

(e) exposing the cells to at least one compound to be tested; and

(f) determining the difference in Notch signalling between cells exposed to the compound to be tested and cells not exposed to the compound,

thereby identifying a compound that modulates Notch signalling.

71. (Withdrawn) An assay for identifying a compound that modulates Notch siganlling comprising the steps of (in any order):

(a) providing a culture of immune cells;

(b) optionally transfecting said cells with a Notch signalling reporter construct;

(c) transfecting said cells with (i) a nucleic acid encoding Notch, (ii) a constitutively active truncated form of Notch or (iii) a Notch IC domain;

(d) optionally providing a Notch ligand;

(e) exposing the cells to at least one compound to be tested; and

(f) determining the difference in Notch signalling between cells exposed to the compound to be tested and cells not exposed to the compound,

thereby identifying a compound that modulates Notch signalling.

72. (Withdrawn) The assay of claim 70, further comprising the step of activating the immune cell.

73. (Withdrawn) The method of claim 65, wherein Notch signalling is monitored by monitoring cytokine production.

74. (Withdrawn) The method of claim 65, wherein Notch signalling is monitored by monitoring IL-10 production.

75. (Withdrawn) The method of claim 65, wherein Notch signalling is monitored by monitoring TNF production.

76. (Withdrawn) The method of claim 65, wherein Notch signalling is monitored by monitoring IFN gamma production.

77. (Withdrawn) The method of claim 65, wherein Notch signalling is monitored by monitoring IL-5 production.

78. (Withdrawn) The method of claim 65, wherein Notch signalling is monitored by monitoring IL-13 production.

79. (Withdrawn) An immune cell transfected with:

(a) a Notch signalling reporter construct; and

(b) (i) an expression vector encoding Notch, (ii) a constitutively active truncated form of Notch or (iii) a Notch IC domain.

80. (Withdrawn) The immune cell of claim 79, wherein the cell is transfected with an expression vector encoding a constitutively active truncated form of Notch.

81. (Withdrawn) The immune cell of claim 79, wherein the cell is transfected with an expression vector coding for a Notch IC domain.

82. (Withdrawn) The immune cell of claim 79, wherein the cell is stably transfected.

83. (Currently amended) A method for identifying a modulator of Notch ~~signalling~~ signal transduction comprising the steps of

(a) monitoring ~~Notch signalling in a cell of the immune system~~ levels of one or more cytokines produced by activated T-cells in the presence and absence of a candidate modulator having a molecular weight of less than about 1000 Daltons as determined by SDS-PAGE, wherein the cytokines are selected from the group comprising IL-5, IL-10, IL-13, and IFN gamma, and

(b) determining whether the candidate modulator modulates ~~Notch signalling,~~ the levels of one or more cytokines, thereby identifying a modulator of Notch signalling.

84. (Currently amended) The method of claim 83, wherein the candidate modulator has a molecular weight of less than about 500 Daltons.